# The Neuroscientist Who Lost Her Mind

MY TALE OF MADNESS AND RECOVERY

BARBARA K. LIPSKA

with ELAINE MCARDLE



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### Prologue

من نفونه بوځی ور من نفونه *m running and running and running*. For hours, T've been running. I want to get home but I have no idea where that is, even though I've lived in this neighborhood for twenty years. So I keep running.

I'm roaming these tree-lined streets in suburban Virginia at a fast clip, wearing my usual outfit—a tank top and running shorts. I sweat as my pace increases, faster, then faster still, my heart pounding but my breath even and unhurried as I sail past large homes with two-car garages and bicycles parked in driveways.

It's the end of spring 2015 and the beginning of what will become a particularly hot and humid summer. The grass on the immaculately trimmed lawns is still green and lush. Pink and white peonies are in full bloom, and all around me azaleas explode in a rainbow of colors.

I've jogged this route hundreds of times over the past two decades. I should recognize each maple tree and camellia bush on each street corner, and every gash in a curb where a teenage driver took a corner too fast. They should be landmarks as familiar to me as anything in my life. But today it's as if I've never seen them before.

When my husband and I bought our home here twenty-five years ago, just two years after leaving the grimness of Communist Poland, this normal American suburb seemed a dream come true. What luxuries it contained! Settled into our new home, we quickly adopted a middle-class American lifestyle, complete with regular meals of Chinese takeout and buckets of ice Cream—indulgences that were nonexistent in Eastern Europe.

One day, I saw a photo of myself-arms chubby and dimpled, thighs spread across my chair-and was shocked into a major lifestyle change. I needed to get more exercise, and I began to run. Not one for minor shifts in my life, I decided I would enter a race as soon as I was able.

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At first, I couldn't jog a single block. Within a year, I was running three منز: نفوزه وزم نخوذه وزم وز miles. After two years, I signed up for my first race, a six-mile competition where I finished at the top of my age group. Since then, my entire family has become dedicated athletes. Runners, cyclists, and swimmers, we're always training for one competition or another.

And so, each morning, I run.

A creature of routine, I always start by taking my German-made prosthetic breast from the shelf in my bathroom. I've worn the breast ever since undergoing a mastectomy following a battle with breast cancer in 2009. Fashioned from high-tech plastic, it is flesh-colored and feels like a real breast, and it is proportioned to match the breast on my right. It even has a tiny nipple. Engineered for athletes, it's light and has a special adhesive on the underside to hold it on to my body. Every morning before my jog, I slap it into place on the smooth, flat skin of my left chest before donning my clothes and sneakers. And then I'm off.

But this morning—this morning—began differently.

After pouring my usual glass of water, I headed into the bathroom and peered at myself in the mirror.

ered at myself in the mirror. My roots are showing, I thought. I need to dye my hair. Now!

I mixed the dye—a brand of honna from Whole Foods that gives my hair a funny purple tint that I love  $\rightarrow$  in a small plastic cup, then squirted it onto my scalp and spread it over my head. I pulled a plastic bag over my skull and tied it with a little knot on one side to hold it in place.

*I must hurry. It's urgent—urgent!—to get outside and begin running!* 

I grabbed my shirt and shorts and headed back into the bathroom.

I looked at the breast on the shelf.

No. Too much trouble. It weighs me down. I'm not going to spend precious time on stupid things like that.

I quickly pulled my tight-fitting shirt over the plastic bag on my head. My body was noticeably lopsided without the prosthetic breast, but I didn't think twice about it.

I need to leave now!

Purple-red dye oozed down my face and neck as I sprinted out of the house and down the street.

is start ei Now, as I run along in the morning heat, the dye spreads over my shirt and stains my asymmetrical chest.

The streets are almost empty in our sleepy neighborhood. If any of the منن نفونه وي بو خرى ف few people I do pass are surprised by my strange appearance, I don't notice. I glide along, absorbed in my own internal world.

After an hour I begin to tire and I am ready to return home. But my neighborhood looks strange. I don't recognize these streets. I don't recognize these houses.

I have no idea where I am. So I keep moving.

It's preposterous that I could get lost in this familiar place, but that fact barely registers in my mind. With no plan for where I'm headed, I simply continue to run.

For another hour or more, I jog along, misshapen and covered in gore. I'm oblivious, unaware of anything amiss. I just run and run, my thoughts drifting into open spaces and big skies.

Somehow, I finally come upon our two-story Colonial. I open the door and find myself in the cool, dark hallway. Tired and sweaty, I take off my sneakers and socks, which are completely soaked.

On my way upstairs, I catch a glimpse of myself in a mirror. My head is caked in sweat mixed with hair color, the plastic bag plastered on top like a weird swimming cap. Streaks of purple dye, long since dried to black, have crusted in thin rivulets down my neck and upper arms and all over my shirt, accentuating the sunken left side of my chest. My face is deep red from exertion.

Nothing strikes me as unusual. I continue past the mirror up the stairs.

In his home office, my husband, Mirek, is sitting at his computer with his back to the door. When he hears me enter the room, he says, "You've been away a long time. Good run?"

Then he turns to me with a smile—and freezes.

"What happened?" he exclaims.

"What do you mean?" I say. "It was a long run."

"Did anybody see you like this?" He seems shaken.

"Why would I care if someone saw me? What are you talking about?"

Wash it off," he says. "Please."

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"Calm down, Mirek! What are you going on about?" But I head into the bathroom to do as he asks.

What's wrong with him? Why is he acting so strange?

I emerge from the shower clean and relaxed. But something nags at me. *The man I love is alarmed. But why?* 

Mirek's behavior should be a red flag, a clue that something is terribly wrong. But a moment later, the unpleasant thought simply slips through the

. unt a neuroscientist. For my entire career, I have studied mental illness, first in my homeland of Poland and then, since 1989, in the United States, at the National Institute of Mental Health (NIMH), a division of the Nation of the Nation of the States of Health (NIH) in Bethesda, Maryland Maryland Maryland is discerning what is real and what is not.

In June 2015, without warning, my own mind took a strange and frightening turn. As a result of metastatic melanoma in my brain, I began a descent into mental illness that lasted about two months, a bizarre tailspin that I couldn't recognize at the time. I emerged from that dark place through a combination of luck, groundbreaking scientific advances, and the 53 vigilance and support of my family.

I'm a rare case; I lived through a terrifying dive into brain cancer and mental illness and emerged on the other side able to describe what had happened to me. According to psychiatrists and neurologists-medical doctors who specialize in the brain and nervous system—it's highly unusual for someone with such serious brain malfunction to be successfully treated and return from the shadowy world of mental impairment. Most people with as many brain tumors as I had and the serious deficits they caused simply don't get better.

As frightening as my breakdown was, I regard it as a priceless gift for a neuroscientist. I studied the brain for decades and conducted research in mental illness, but my brush with madness gave me firsthand experience of what it's actually like to lose your mind and then recover it.

Every year, approximately one in five adults worldwide experiences a mental illness, from depression to anxiety disorders, from schizophrenia to bipolar disorder. In the United States, mental illness affects nearly fortyfour million adults each year, and that number does not include people with substance-abuse disorders. In Europe, 27 percent of adults experience a serious mental disorder in any given year. Mental illness often emerges during young adulthood and lasts for someone's entire life, causing tremendous suffering for the person who is ill as well as for his or her loved ones. A significant number of homeless and incarcerated people suffer from

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mental illness, and the societal consequences do not end there. Mental illness costs the global economy \$1 trillion each year—\$193.2 billion in the United States—as people who would otherwise be productive are unable to function because of their disabilities. More than just incapacitating, mental illness can also be deadly. Of the roughly 800,000 people worldwide who die each year by suicide—41,000 in the United States alone—90 percent suffer from mental illness.

The United States spends significantly more on treating mental disorders than it does on any other medical condition—a whopping \$201 billion in 2013. (Heart conditions, for which the U.S. spent \$147 billion that year, rank a distant second.) But even with these resources and the tremendous efforts of dedicated scientists and physicians, mental illness remains deeply enigmatic, its causes generally unknown, its cures undiscovered. Despite the overwhelming body of research on mental illness to which new findings are added almost every day, we scientists still don't understand what happens in the brains of mentally ill people. We don't really know yet which brain regions and connections are malformed or undeveloped or why the brain goes awry. Are people who become mentally ill destined to suffer because of some genetic predisposition, or did they experience something that broke their brains, mangled their neuronal connections, and altered their neurologic function?

Today, the data suggest that mental illness is caused by a combination of heredity and environment, the latter involving multiple factors—including drug use and abuse—that act in complex interplay with one another and with our genes. But it remains exceedingly hard to pinpoint the biological and chemical processes for mental illness, in part because these disorders are diagnosed through observations of behaviors rather than through more precise tests. Unlike cancer and heart disease, mental illness has no objective measures—no biological markers that we can see on imaging scans or determine through laboratory tests—to tell us who is affected and who is not. In the aggregate, groups of people who suffer from mental illness may show differences in their brain structures or functions, but for now, individual patients can't be diagnosed using conventional measures such as blood tests, computerized tomography (CT) scans, or magnetic resonance imaging (MRIs).

Diagnosing mental illness is all the more difficult because the constellation of symptoms not only varies from person to person but also

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often fluctuates over time within an individual. Not everyone afflicted with schizophrenia screams in distress, for instance; some people with the disease may shut down and stop communicating. Likewise, people with dementia may be attentive and engaged one minute and detached and withdrawn the next. Even more challenging, some indications of mental illness may be exaggerations of normal personality traits, making the behaviors particularly hard to recognize as pathological. With people who are naturally frank and outspoken, the lack of judgment that can accompany dementia may at first be construed as their typical bluntness. Similarly, when introverted people become more withdrawn, others may not realize that they are exhibiting symptoms of Alzheimer's disease.

For researchers, it's becoming clearer that specific mental disorders are not well-defined categories of illness, each delineated by a distinct set of symptoms and biological indicators. The same symptoms may not even be caused by the same illness, so two people who exhibit the same erratic behavior may in fact be suffering from two completely different disorders. Or perhaps there is overlap among various mental disorders in terms of symptoms, biological mechanisms, and causes. Some genetic and clinical analyses find similarities across a wide variety of diagnoses, suggesting that mental illnesses share a common neurobiological substrate. Modern science is currently exploring this possibility.

Today, scientists are quite confident that the main site of disruption in people with mental illness is the highly evolved prefrontal cortex, which sits at the front of the brain, and its network of connections with other parts of the brain. But what these abnormalities are and how exactly the brain malfunctions in various mental problems remains a puzzle.

When a person's behavioral changes are triggered by brain tumors, as mine were, it may seem easy to establish a cause-and-effect relationship between neurological factors and behaviors. Neurologists like to try to localize every problem to a particular part of the brain, and sometimes that's more or less possible. But metastatic brain tumors—whether from melanoma or breast cancer or lung cancer—tend to involve multiple parts of the brain at the same time. When you have two or more tumors, as I did, it becomes especially difficult to figure out what part of the brain is affecting what behaviors. In addition, when there is extensive swelling from tumors and treatments, the entire brain contributes to the altered behavior.

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While we don't know exactly what took place in my brain or where precisely it happened, my journey has given me an invaluable opportunity to tour the landscape of the brain. As a result, I've come to better understand this breathtakingly complex structure and its incredibly resilient product: the human mind.

As with everyone who suffers from mental disorders, I experienced a constellation of symptoms during my brush with madness that were unique to my case. But during my brief mental breakdown, I exhibited many symptoms described in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (*DSM*-5), the official guide clinicians and researchers use to classify various mental illnesses. For that reason, the similarity between my experience and that of people with a wide range of mental illnesses—from Alzheimer's to other dementias, from bipolar disorder to schizophrenia—is remarkable. Identifying these parallels and using them to better understand the experience and causes of mental illness is one of my main goals in this book.

I gained a deep understanding of what it is like to live in a world that makes no sense, that's bewildering and unfamiliar. I know what it's like to be so confused that you trust no one, least of all those closest to you, who you may be convinced are conspiring against you. I know how it feels to lose not only the powers of insight, judgment, and spatial recognition but also the faculties essential for communication, such as the ability to read. Perhaps most chilling, I also know what it's like to be completely unaware of these deficits. It was only after my mind began to return that I learned how warped my reality had been.

After I emerged from that dark space and was given a second chance at sanity, I wanted to explore, as a neuroscientist, what went wrong in my brain. I learned that my frontal and parietal lobes—which are responsible for many of our most human behaviors—were malfunctioning. This helps to explain why I behaved in ways similar to people with mental illness: why I got lost in familiar places, forgot things that had just happened to me, and became angry, mean, and unloving to my family; why I became obsessed with strange little details like what I was having for breakfast while ignoring the fact I was about to die; and, most striking, why I failed to notice any of these insidious changes in myself. Even as my mind was deteriorating, I couldn't see that I was slipping into mental illness.

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In addition to providing insight into mental illnesses such as schizophrenia and dementia, my experience gave me a greater understanding of other brain disabilities, including the mental declines that many of us encounter as we age. Many people may someday face in themselves, their partners, or their parents the bewildering mental changes I had—memory loss, disinhibited and inappropriate behaviors, altered personality, and the inability to recognize these problems in oneself. The frontal cortex, the part of my brain that was most affected by my tumors and treatment-induced swelling, is one of the regions that often begin to fail as we enter our senior years (the hippocampus is another). It's one of the many ironies of my story that if I live long enough to see old age, there's a good chance I will experience many of the same mental changes all over again.

In the course of losing and regaining my sanity, I've come to identify with other people who have known mental illnesses firsthand. This sense of connection with others who suffer has spurred me to share my story. While more attention is being given to mental illness than ever before, it nonetheless continues to be stigmatized by society. Even though mental disorders are physiological in nature—they are diseases of the brain, just as coronary problems are diseases of the heart—the mentally ill are often treated as if *they* are to blame, as if *they* have done something wrong. Their families are frequently stigmatized as well. If nothing else, I hope my experience helps others recognize that mental illness is no more the patient's fault than cancer is and that the best response to mental illness is empathy and a greater commitment to finding cures.

After losing my mind and regaining it, I like to think I am more attuned to other people's feelings and troubles, that I am more understanding as a mother, wife, friend—and scientist. While I believe that I've always been compassionate toward people with mental illness, since my own brush with madness, the quality of my compassion has deepened. I also live my life more consciously, aware of how lucky I am to be reunited with my family and able to continue my life's work.

This book is an account of what mental illness looks like from the inside. But it is also a map of my evolution as a scientist and a person. It is the story of an incredible journey, one from which I could not have imagined I would ever return. It is a story that I never thought I would be able to tell, of

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### The Rat's Revenge

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As director of the Human Brain Collection Core at the National Institute of Mental Health, I work surrounded by brains; a library of brains, a bank of brains, a compendium of brains that for any number of reasons hadn't worked the way they should have. Brains that saw hallucinations, heard mysterious voices, were buffeted by wild mood swings, or were deeply depressed. Brains that have been collected, cataloged, and stored here for the past thirty years.

About a third of these brains come from suicides. That desperate and heartbreaking act is the ultimate cost for so many people who suffer from mental illness, and my colleagues and I are reminded of this grim fact each and every day.

Each specimen arrives to us fresh and bloody, glistening inside a clear plastic bag placed carefully inside a cooler of ice. It looks like a piece of red meat, unconnected to any real humanness. Yet just a day earlier, it had directed every movement and thought of the person from whom it came.

To understand mental illness—and to treat and one day cure it researchers need a steady supply of brains. This is where institutions like the NIMH, the leading federal agency in the United States for research on mental health, come in. At the brain bank, we gather these incredible organs, slice them into usable tissue samples, and share them with scientists around the world.

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But collecting brains isn't easy. It's especially difficult to get brains that come from people with schizophrenia, bipolar disorder, major depression, anxiety disorders, and addictions to various substances—cocaine, opioids, alcohol, and even cannabis—that attract abuse. What's more, we can't use brains of mentally ill people who died of serious illnesses, who were in hospitals on ventilators, or who were heavily medicated before taking their last breath. Brains marked by other illnesses or medical issues would only add complexity to the already overwhelming puzzle that we are trying to solve: What causes mental disorders?

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In order to begin to understand this, we also need brains from people without mental illness (control brains), so we can examine and compare them with diseased brains. In short, we need clean and healthy brains both with and without the terrible presence of madness.

We get most of our brains from the morgues in nearby medical examiners' offices, where bodies typically arrive because people have died under suspicious or mysterious circumstances. And so, in addition to receiving the brains of suicides, we are also the unintentional beneficiaries of homicides and unexplained deaths.

First thing each morning, the technicians in our brain bank telephone local medical examiners' offices and ask, Do you have any brains for us today?

We're in a rush. If a person has been dead more than three days, we can't use the brain. We need the brains before the tissue begins to decompose, before their proteins and other molecules, the ribonucleic acid (RNA) and deoxyribonucleic acid (DNA), begin to break down, rendering them useless for molecular studies.

The morgue workers tell the techs about the bodies that have arrived in the past twenty-four hours, sharing what information they have. Often, it isn't much, just the barest of facts: A young man who overdosed on heroin. A middle-aged woman with a heart attack. A teen who hanged herself. At this point, it may be all we know about each person.

Once the technicians have compiled their list of candidates, they come to me, and together we narrow it down. Do we want this one, a drug overdose? Or this one, an elderly man whose wife told morgue investigators he was an alcoholic? Here's a man who died in a car accident. There's no indication he had mental illness, so maybe researchers will be able to use his brain as a

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control in their studies. But he might have sustained a head injury; do we still want him?

If there's any possibility that a brain may be right for us, I usually say yes. The brains we seek are rare and precious, and we don't get nearly enough.

لنن فعونه وي چې چې د چې چې Once we have settled on potential candidates, our technicians contact each one's next of kin to make a wrenching request: Would you consider  $\checkmark$ donating your loved one's brain to medical research?

It seems a simple question. Yet a few hours earlier, these people were alive. Now they are forever lost, and we are asking parents or spouses or children to see through their own shock and grief to give us the most personal part of their loved ones, the part that made up the very essence of who they were. Not surprisingly, perhaps, only about a third of them agree to donate the brains we seek.

When a brain arrives at our bank, we label it with a number in order to protect confidentiality. Then our job begins in earnest. We can now cut this specimen open and study its inner workings in an attempt to better understand mental illness.

It is among these brains—sliced up and frozen in a slurry of hope and optimism that they will one day reveal their secrets-that I do my work.

Brains are a bloody business. Pve worked with them for over thirty years, starting with rat brains, each of which is the size of a walnut, smooth, and relatively simple. They have none of the intricate folds and crevices-called gyri and sulci—of the human brain.

By contrast, the human brain is large, elaborate, and far more complex. It is a feat of evolutionary engineering. All of its folds, all of those gyri and sulci, ridges and crevices, help to squeeze more storage and function into the relatively small space of the human skull. Consciousness is one of the many products of this marvelously complicated piece of tissue.

Unfortunately, mental illness—an affliction of consciousness—is a product as well.

In our quest to understand what's wrong in the brains of people with mental illness, we have to dig deep into the brain's tissues, cells, and molecules. Novel techniques make this a little easier every year. To try to unlock the secrets of schizophrenia, for instance, I examine thin slices of brain stained with radioactive or fluorescent dyes and evaluate the cells'

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various molecules, proteins, and types of RNA and DNA. To read their genetic code, I analyze the brain cells' minute molecular composition with modern sequencing machines.

لنن نفوند. ج ج ج ج As a neuroscientist and molecular biologist, I'm an expert on the brain. But I'm not a clinical doctor. Before I became head of the brain bank, I'd never worked with intact human bodies or even identifiable body parts. I did my work in quiet laboratories far from morgues and hospitals, and by the time the brains got to me, they didn't look like brains at all. They were pulverized bits of frozen tissue that looked like specks of pinkish flour suspended in liquid in little test tubes, or they were thin slices of tissue preserved in foul-smelling chemicals. They could have been almost anything or come from almost any organism.

It never bothered me to be both intimate with and distant from the subjects of my studies. After all, that is the nature of scientific research. Each scientist works on her own small, discrete piece of an overwhelming puzzle that she hopes will someday be solved by researchers' collective efforts and to which her narrow contribution will have been some significant part.

Before I took this job, I'd never even touched a whole human brain. I'd been to a morgue several times, seen bodies splayed open with their organs removed. But I'd never seen a brain lifted out of a skull. I'd never held a whole brain in my hands, much less cut one apart.

"You have to do it yourself," my predecessor at the brain bank, Dr. Mary Herman Rubinstein (known as Dr. Herman), urged me in 2013 as she trained me. "When we get the next brain, we'll slice it up and freeze it together."

So we do. On a sunny day in September of that year, with the leaves just beginning to turn yellow and red but the air still warm and comforting, we stand in the lab awaiting the arrival of my first brain. We are armored in protective gear—surgical masks strung from ear to ear, plastic shields over our faces, hair caps secured tightly around our foreheads, several layers of latex gloves that cover our arms up to our elbows, white lab coats overlaid with plastic aprons to protect us from splashing blood, and plastic booties covering our shoes.

A technician carries in a large white cooler, the kind that holds beer and steaks for a football tailgate party. This cooler, I know, contains a human brain packed in lots and lots of ice.

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It is critical that the brain stays cold, because this helps slow the process by which tissues break down. For our experiments, the brain cells' RNA key to how genes are expressed—must be intact. Putting a brain on ice immediately after it's removed from the body is the first step in preserving the RNA, but for long-term storage, we must quickly deep-freeze the tissue. Keeping the brain at very low temperatures can halt RNA decomposition for decades.

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Dr. Herman opens the lid of the cooler and carefully lifts out a clear plastic bag frosted with ice. She slowly takes out the brain and places it in my outstretched palms. It fits comfortably in my hands. Heavy, cold, and wet, it drips with blood just like any other piece of meat. The average brain weighs 1,300 grams, or about three pounds; in time, I will see some that are as large as 1,800 grams, about four pounds. It feels like firm Jell-O, but in fact it's quite fragile; if I'm not careful, parts might snap off.

Given that the human brain is the most complex structure in our universe, you'd expect it to look more . . . well, complicated. But it just doesn't appear all that extraordinary. The first time I saw a dead body in a morgue —all the blood, muscles, bones, and skin—I was afraid I would faint. But I find the brain now in my hands much less disturbing. Removed from the body in which it grew, this brain seems almost nonhuman.

Yet the enormous contrast between this ordinary-looking piece of meat and the complexity within it is deeply moving. It is awe-inspiring, marvelous, to realize that everything about a human being can be contained in my hands.

This brain governed a person who was alive less than a day ago. That much I'm sure of. But what else can I know about the brain that I hold? Did it come from a woman or a man? Did this person suffer from mental illness? Did this person kill him- or herself? The likelihood of that is high, given where we get these brains. But it's also entirely possible that the brain came from an elderly woman who died of pneumonia or a young man who was killed by a gunshot wound to his chest. The person might have suffered from schizophrenia or depression, but he also might have had a clean bill of mental health. There is no way to know from looking at it with the naked eye. The brain does not reveal its secrets easily.

A whole brain is shaped somewhat like a football and is divided by a deep groove down the middle into a left and right hemisphere. Each hemisphere has four lobes: the frontal, temporal, parietal, and occipital.

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As I hold this brain in my hands, I stare at the frontal lobes, the largest of the lobes. These regions of the cerebral cortex, the outer covering of the brain, determine much of our species' conscious existence, from our perceptions of the world to our most private thoughts and imaginings. They are the parts that fascinate me the most and that preoccupy the overwhelming majority of neuroscientists.



The frontal lobes—one on the left, one on the right—extend from the bottom of the forehead, right above the eyes, all the way back to the top of the skull. Like the other lobes, they're wrapped around the more primitive parts located farther inside the brain.

I linger over the frontal cortex, the front top part of the frontal lobe, situated roughly where the hairline is. Large and full of folds and crevices, it is both the youngest and the most evolved part of the human brain. It determines who humans are—thinking, remembering, problem-solving creatures capable of judgment and informed decision-making.

The prefrontal cortex, the foremost part of the frontal cortex, sits just behind the forehead. This relatively small part of the cortex is perhaps the most crucial to our sanity because the prefrontal cortex controls what is known as executive function—the most complex cognitive tasks, such as

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the ability to differentiate between right and wrong, inhibit inappropriate or impulsive behavior, and predict the future consequences of things that happen in the present. Extensive research into the neuroscience of mental illness leaves little doubt that problems of the prefrontal cortex are central to mental illness. But we don't know what kinds of problems they are, and just by looking at this brain's frontal cortex, I certainly can't tell.

Behind the frontal lobe, separated by a deep sulcus, or groove, I spot the parietal lobe, another large chunk of convoluted cortex. The parietal lobe coordinates sensory information sent to the brain from the rest of the body, allowing us to feel, taste, move, and touch. It places us in space, tells us where we are in relation to things around us, and where our bodies start and end. It also enables us to read and do math.

I turn the brain on its side and peek at the temporal lobe, which lies behind the temple, roughly above where the ear is. This part of the cortex is responsible for high-level auditory processing, for hearing and understanding speech. Beneath it, deep inside the brain, hidden from my eyes and surrounded by layers of cortical tissue, sits the hippocampus, named from the Greek word for "seahorse" because of its unusual curved shape. An evolutionarily primitive part of the brain, the hippocampus stores long-term memories. It also works like a GPS, enabling spatial navigation so we know where we are.

Hidden at the back of the brain is the exquisitely ribbed cerebellum, made of densely packed neurons. It coordinates voluntary movements: how we sit, walk, and speak. Just above it, where one would tie a ponytail, is the fourth and final lobe, the occipital lobe, the structure that processes information from the eyes and enables us to see.

All of the brain structures are enormously important to everyday functioning. If you injure the brain stem at the back of your brain—the part that regulates breathing, heart rate, and other basic functions—you could be paralyzed, or die. But the frontal cortex is perhaps the most precious brain region of all. While a person won't die without a frontal cortex, it is the part that makes us human. Damage to this region of the brain results in a large number of adverse symptoms, from memory loss to the inability to plan and organize actions, from problems with language and speaking to inappropriate behavior and poor judgment.

I would be happy to linger longer in admiration of this brain, the first I've ever held, but Dr. Herman and I must work quickly to preserve the

specimens for our studies.

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I carefully place the brain on a large board that sits atop a bed of ice and pick up the dissecting knife, which is very long with a razor-sharp edge.

Loss sharp edge. Loss Dr. Herman instructs me. "Keep Loss with the top surface of the brain, and try to Loss each cut parallel to the previous one." Holding the brain with my left hand, I lift the knife and then begin to ce. The cold storage has made the tissue firm, and the knife slides ough easily. My first cut is longitudinal alor b hemisphere the knife's edge perpendicular to the top surface of the brain, and try to make each cut parallel to the previous one."

slice. The cold storage has made the tissue firm, and the knife slides through easily.

two hemispheres. I then slice into the left hemisphere, from front to back, creating uniform slices about half an inch thick. After a while, I feel the brain becoming mushy as it warms. Instead of falling neatly onto the cutting board, the slices fold over and crumple. I continue, though, getting better with each cut.

I pick up and examine each slice, and Dr. Herman points to its folds and creases and the borders marked by different tones of pinkish gray or white. These delineate subregions of the brain, the gray, neuron-rich areas and the white connecting fibers that run between them. Depending on where a given slice is, a particular specimen may include parts of the hippocampus, the amygdala, or some other structures inside the brain.

We quickly place each slice on a glass plate and immerse it in a mixture of dry ice and a volatile chemical called isopentane—a slurry with a very low temperature of minus 86°C. The semiliquid mixture steams and bubbles violently as we slide the tissue into it, and the slice freezes instantly, turning in seconds from bloody pink to frosted white. This procedure preserves the anatomy of the slice, preventing cell membranes from bursting open as they would during a slower freezing process. We promptly fish it out with forceps and place it in a plastic bag that we seal shut and label with a printed barcode. The preservation process is now complete.

If this brain initially resembled an ordinary piece of meat, it now looks like a stack of cold cuts in a grocery store's deli case. As if to reinforce that rimpression, white-coated technicians arrive to ferry the cut-up samples to our laboratory's deep freezer. There the specimens will sit, cold and silent, until they can be employed in our endless quest to discover the brain's secrets.

Human brains are exquisitely complex, but we can learn a great deal about them by studying creatures with brains vastly simpler than our own, as I found out early in my scientific career.

منز: نفونده چوند بود. Thirty years before I became the leader of the brain bank at NIMH, I was a young research scientist at the Institute of Psychiatry and Neurology in Warsaw with a master's degree in chemistry and a PhD in medical sciences with a focus on the brain and nervous system. In the mid-1980s, I was working on clinical trials of drugs manufactured by Western companies to treat schizophrenia and living in a small apartment in Warsaw with Mirek, my then boyfriend, and my two young children from my first marriage.

In August of 1988, our lives were upended. That month, at the invitation of a German pharmaceutical company, I attended the International Congress of Neuropsychopharmacology in Munich. I was to present a poster on certain antipsychotic drugs designed to reduce the severity of hallucinations and psychosis, the most distressing symptoms of schizophrenia. I had no way of knowing that my focus was soon to shift from treating this terrible disease to hunting for its underlying causes  $45^{\circ}$ 

I arrived in Munich with no more than twenty dollars in my pocket—an entire month's salary-and was immediately dazzled by the opulence of West Germany. But my culture shock paled in comparison to the thrill I experienced when, at the conference, I was approached by Dr. Daniel R. Weinberger, an NIMH psychiatrist who was world-renowned for his studies on schizophrenia. No sooner had we met than Dr. Weinberger offhandedly suggested I come work as a postdoc in his lab.

I could hardly believe my luck. NIH was the most prestigious medical institution in the world, and its mental-health division was at the forefront of global research on the very illnesses that I'd devoted my career to studying. I'd never dared to dream that I might someday end up at NIMH myself. 5°

A few days later, I returned to Poland and proudly announced to Mirek and my children that we were going to America! They were just as excited as I was. Poland at the time was looking bleaker and more unstable than ever, and many of its unhappy citizens dreamed of the freedom that the West offered. And everyone knew that American society was the freest of them all.

I arrived in the United States ahead of my family, in the spring of 1989, just as Poland was tipping toward democracy and threatening to bring the

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rest of the Soviet bloc down. The day after my arrival, Dr. Weinberger-559.25 who would be my boss for the next twenty-three years—drove me to the NIH campus and introduced me to Dr. George Jaskiw, a psychiatry fellow from Canada. Dr. Jaskiw became an enthusiastic mentor to me, and together we began to explore the mysteries of the same disease—schizophrenia that I had studied in drug trials in Warsaw.

Dr. Jaskiw and I worked on rats because their brains are similar to human brains in their structure, although not nearly as sophisticated, and because rats display complex behaviors, such as working memory, cognition, and social behaviors, that are useful in understanding humans. We first focused on creating slight defects in the hippocampi of living rats because robust research data at that time suggested that the hippocampi in humans with schizophrenia were structurally abnormal and therefore did not function correctly. To disrupt the connections between the hippocampus and the prefrontal cortex in the brains of newborn rats, we injected minute amounts of neurotoxins into the hippocampus. In this way, we created brains with faulty wiring between these two areas critical in schizophrenia. We wanted to see how different our neurologically altered rats would be from normal animals and, especially, how they would behave when they grew up.

I'd never sliced into any creature, living or dead, but I was delighted to be part of this work. We threw ourselves into the experiments with the crazed abandon of knowledge-hungry scientists. Once, when I needed a quiet area to conduct our rat-behavior experiments, I placed my rats in their testing cages on the floor of the men's restroom, taped up a sign that said EXPERIMENT IN PROGRESS! DO NOT ENTER, and locked the door. I was determined to learn and succeed. Dr. Jaskiw taught me neuroanatomy and neurochemistry, rat physiology, and the best techniques for brain dissection. Together we operated on and tested thousands of rats.

After eighteen months, and much to my dismay, Dr. Jaskiw left NIH for another career opportunity. Without him, my work became much more structures in rodent brains, use our lab's finicky slicing machines, and catch

As painful as Dr. Jaskiw's departure was, it forced me into independence expected, this scientific breakthrough concerned the frontal cortex, the same